

Attorney Docket No. P66351US0
Application No. 09/774,178

Remarks/Arguments:

Claims 11 and 19, previously presented, are pending.

Claims 1-10, 12-18, and 20-22 are canceled, without prejudice or disclaimer.

Claims 11 and 19 were rejected under 35 USC 103(a) as allegedly being unpatentable based on *Nucleic Acids Research*, 26, 1854-1855, 1998 (Nakahara) in view of US5654142 (Kievits), *Nucleic Acids Research*, 26 (1998), 2150-55 (Leone), and *Methods in Molecular Biology*, 38 (1994), 253-60 (Malek). Reconsideration is requested.

The rejection relies on four, separate prior art references. According to the rejection, each of the cited references separately discloses limitations found combined in the present rejected claims. The rejection alleges that one of ordinary skill in the art would have found it obvious to select, from among all the teachings in all of the cited references, just those teachings that match the claim limitations and combine those teachings as the limitations in the claims are combined. As for claim limitations not found in the cited references, the rejection alleges that the missing limitations would have been obvious optimizations of features that are found in the cited references. The rejection is incorrect.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art," *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970), "and it is error to ignore specific limitations distinguishing over the [prior art] reference." *Ex parte Murphy*, 217 USPQ 479,

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481 (PO Bd. App. 1982). When obviousness is grounded on a claim limitation (absent from the prior art) allegedly being an "optimization which is highly desirable," the "ground of rejection is simply inadequate on its face . . . because the cited references do not support each limitation of [the] claim." *In re Thrift*, 63 USPQ2d 2002, 2008 (Fed. Cir. 2002).

The "evidence upon which the examiner relies must clearly indicate that a worker of routine skill in this art would view the claimed invention as being obvious." *Ex parte Wolters*, 214 USPQ 735, 736 (BPA&I 1982). "It is facts which must support the legal conclusion of obviousness." *Ex parte Crissy*, 201 USPQ 689, 695 (POBdApp 1976).

The Patent Office has the initial duty of supplying the factual basis for its rejection. It may not, because *it may doubt* that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis.

In re Warner, 154 USPQ 173, 178 (CCPA 1967) (*emphasis in original*).

In the context of a rejection for obviousness under §103, the "*Examiner* bears [both] the initial burden . . . of presenting a *prima facie* case of unpatentability" and "the ultimate burden of persuasion on the issue." *In re Oetiker*, 24 USPQ 1443, 1444 and 1447 (Fed. Cir. 1992) (*emphasis, added*). "The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art *would lead* that individual to combine the relevant references. . . . Indeed, the teachings of the references can be combined only if there is some suggestion or incentive to do so." *Ex parte Obukowicz*, 27 USPQ 1063, 1065 (BPA&I 1992)(*emphasis, added*).

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As explained by the Board in the decision *Ex parte Levengood*, 28 USPQ2d 1300, 1300-01 (BPA&I 1993)(*emphasis in original*):

In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*,^[1] preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, that one having ordinary skill in the art *would have been led* to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention [*citations, omitted*].

The fact that all elements of a claimed invention are known does not, by itself, make the combination obvious. *Ex parte Clapp*, 227 USPQ 972 (BPA&I 1985). (Although the three claimed elements were known, separately, for use in water cooling systems did not support the PTO finding that it would have been obvious to use them together but, at best, obvious to try various combinations. *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987)).

When the claimed invention requires modification of the prior art, there is no obviousness under §103 when "[t]he prior art does not suggest . . . [the] modification . . . or provide any reason or motivation to make the modification." *In re Laskowski*, 10 USPQ2d 1397, 1398 (Fed. Cir. 1989). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988).

It is impermissible within the framework of §103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.

In re Hedges, 228 USPQ 685, 687 (Fed. Cir. 1986).

When prior art references require selective combination by the court to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself. . . There must be "something in

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the prior art to suggest the desirability, and thus the obviousness, of making the combination" [citation omitted].

Interconnect Planning Corp. v. Feil, 227 USPQ 543, 551 (Fed. Cir. 1985).

... it is impermissible to use the claims as a frame and the prior art references as a mosaic to piece together a facsimile of the claimed invention.

Uniroyal, Inc. v. Rudkin-Wiley Corp., 5 USPQ2d 1434, 1438 (Fed. Cir. 1988).

Where the *optimization* of a claim variable was not recognized in the art as effecting the claimed result, the result is unobvious. *In re Antonie*, 195 USPQ 6, 8 (CCPA 1977). That a difference with the prior art amounts to an alleged "optimal condition ... is not a substitute for some teaching or suggestion supporting an obviousness rejection." *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

According to the statement of rejection, Nakahara meets all of the claim limitations except for "the repeating steps using the transcribed RNA" and "wherein the tris-HCl is present at a final concentration of 50mM to 80 mM" and, with respect to claim 19, "wherein the transcribing step occurs in the presence of a fluorescently labeled probe" (Office Action page 3). Further according to the rejection, Kievits (apparently) teaches the claim limitation of repeating steps using the transcribed RNA (absent from Nakahara). Nevertheless, according to the rejection the combined teachings of Kievits and Nakahara, still, fail to meet the claim limitation wherein the tris-HCl is present at a final concentration of 50 mM to 80 mM and the claim limitation wherein the transcribing step occurs in the presence of a fluorescently labeled probe (Office Action, page 4).

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With respect to the claim limitations missing from the combined teachings of Kievits and Nakahara, Leone is relied on as allegedly meeting the limitation (in claim 19) wherein the transcribing step occurs in the presence of a fluorescently labeled probe. Concerning the claim limitation wherein the tris-HCl is present at a final concentration of 50 mM to 80 mM, it would have been an allegedly obvious optimization of the 200 mM final concentration disclosed in Leone. Additionally, the claim limitation on tris-HCl concentration would have been an obvious optimization of tris-HCl concentrations disclosed in Malek.

According to the statement of rejection, one of ordinary skill in the art would have been motivated to (1) combine and (2) optimize the teachings of the cited references, as set forth in the statement of rejection, because (1) each of Kievits and Leone allegedly teaches "a method similar to that of Nakahara" and (2) "for the benefit of optimizing the RNA detection conditions as taught by both Leone . . . and Malek." The alleged motivation for combining the cited references fails to satisfy the standards for showing the requisite prior art motivation needed to sustain a rejection under §103(a).

With respect to the alleged motivation (i.e., desirability) for combining the separate, prior art teachings, the rejection merely relies on the fact that methods disclosed in the cited references are similar to one another. This establishes no more than the fact that the claim limitations found in these references were known, separately, in the prior art; which, at best, supports a finding that it would have been obvious to try various combinations. *Geiger, supra*. The fact that all elements of a claimed invention are known does not, by itself, make the combination obvious. *Clapp, supra*.

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Accordingly, the requisite "desirability, and thus the obviousness, of making the combination" being absent from the cited references, lack of patentability based on the cited references has not been demonstrated. *Interconnect Planning Corp.*, 227 USPQ at 551. With all due respect, the PTO tries "to use the claims as a frame and the prior art references as a mosaic to piece together a facsimile of the claimed invention," which "is impermissible" in an obviousness analysis under §103(a). *Uniroyal, Inc.*, 5 USPQ2d at 1438. Withdrawal of the rejection under §103(a) appears to be in order.

With respect to reliance on the claim limitations being "highly desirable" optimizations of features disclosed in the cited references, this renders the rejection "inadequate on its face." *Thrift*, 63 USPQ2d at 2008. Where the *optimization* of a claim variable was not recognized in the art as effecting the claimed result, the result is unobvious. *Antonie*, 195 USPQ at 8. That a difference with the prior art amounts to an alleged "optimal condition . . . is not a substitute for some teaching or suggestion supporting an obviousness rejection." *Rijckaert*, 28 USPQ2d at 1957. Withdrawal of the rejection under §103(a) further appears to be in order.

Furthermore, the rejection fails to take into account disclosure in the cited references that appear to teach away from the present claims. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, . . . would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

In accordance with the present (rejected) method claims, target RNA is efficiently amplified (using a T7 promoter in tris-HCl buffer) in the presence of, *i.e.*, "3.2 to 4.4 mM" inosine triphosphate

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(ITP), in terms of the final concentration. The rejection relies on modifying Nakahara in view of Kievits; but the fact remains that Nakahara and Kievits disclose optimal ITP concentrations for RNA amplification at 2.0 mM and 2.5 mM, respectively. As such, since "a person of ordinary skill, upon reading the reference[s], . . . would be led" to use an optimal maximum ITP concentration of 2.5 mM, which is "in a direction divergent from the path that was taken by the applicant," i.e., using a minimum ITP concentration of 3.2 mM, the references teach away from the presently claimed invention. *Gurley*, 31 USPQ2d 1131.

Furthermore, these teachings of the optimal ITP concentration by Nakahara and Kievits mean that RNA amplification is inhibited at final ITP concentrations higher than the optimal ITP concentrations taught by the cited references, as set forth in the previously filed amendment. Thus, from the teaching by Nakahara and Kievits, one of ordinary skill in the art would have never expected that RNA would be amplified more efficiently at ITP concentrations higher than the optimal ITP concentrations taught by Nakahara and Kievits, i.e., ITP concentrations higher than 2.5. mM. The properties exhibited by a claimed invention must be taken into consideration when comparing the claims against the prior art. *In re Estes*, 164 USPQ 519 (CCPA). *See, In re Papesch*, 137 USPQ 43, 51 (CCPA 1963). Where the invention combines elements not combined in the prior art and results in a synergistic effect, i.e., a greater than additive result, this provides a sufficient showing of nonobviousness under §103. *In re Corkill*, 226 USPQ 1005 (Fed. Cir. 1985).

Moreover, from the data shown in present application Figs. 7 and 8, it appears that improvement in amplification efficiency, in the presence of from 3.2 to 4.4 mM of ITP, results in

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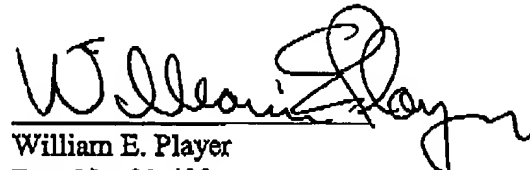
a trivial shortening of the rising time only by a couple of minutes. In other words, a trivial, 1-2 minute shortening of the rising time effects a big difference, when RNA in a sample from human is amplified for the purpose of gene diagnosis. This is because it is necessary, in such a case, to handle (measure) each sample as fast as possible; for example, when 100 samples are measured continuously, a 1-2 minute-shorter rising time for each sample makes a big difference in the total measurement time and the throughput per unit time.

Favorable action is requested.

Respectfully submitted,

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